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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/552,304	07/26/2006	Hairuo Peng	A195 US002	1897

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EXAMINER	
BALASUBRAMANIAN, VENKATARAMAN	
ART UNIT	PAPER NUMBER
1624	
MAIL DATE	DELIVERY MODE
03/27/2009	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/552,304	PENG ET AL.	
	Examiner	Art Unit	
	/Venkataraman Balasubramanian/	1624	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *21 January 2009*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-39* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-22 and 26-39* is/are rejected.

7)☒ Claim(s) *23-25* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *2/9/2007*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

Applicant's election of Group I, claims 1-39 drawn to compound of formula I wherein B is N, B^1 is N and B^2 is N, namely triazolo triazine, composition and method of use, in the reply filed on 1/21/2009 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)). Claims 1-39 will be examined to the extent they embrace the elected subject matter.

Information Disclosure Statement

References cited in the Information Disclosure Statement, filed on , are made of record.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-22 and 26-39 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

1. Recitation of "urea" and "thiourea" in claim 1 renders claim 1 and its dependent claims 2-22 and 26-39 indefinite as it is not clear what is intended. Note urea and thiourea are compounds.

2. Recitation of "urea, thiourea, sulfamoyl, carbamoyl" in claim renders claim 1 and its dependent claims 2-22 and 26-39 indefinite as these groups are bifunctional groups and it is not clear what else is appended to them.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claim 28-39 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for treating Parkinson's disease does not reasonably provide enablement for treatment all or any disease central nervous system diseases, as embraced in the claim language. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

The instant claims 28-31 are drawn to a method of modulating and inhibiting adenosine-A_{2a} receptors while claims 32-39 are drawn to a method of treating or preventing a disorder or disease in which adenosine-A_{2a} receptors are associated with.

Instant claims, as recited, are reach through claims. A reach through claim is a claim drawn to a mechanistic, receptor binding or enzymatic functionality in general format and thereby reach through a scope of invention for which they lack adequate written description and enabling disclosure in the specification.

In the instant case, based on the inhibition or modulation of adenosine-A_{2a} receptors by the instant compounds, instant claims reaches through inhibiting and

treating any or all diseases and disorders in general and thereby they lack adequate written description and enabling disclosure in the specification.

More specifically, in the instant case, based on the mode of action of instant compounds as inhibitor or modulator of adenosine-A_{2a} receptors, based on limited assay, it is claimed that treating or preventing any or all diseases or disorders in general, which there is no enabling disclosure. The scope of the claims include both treating and preventing any or all diseases/disorders due said mode of action for which there is no enabling disclosure.

Reading from specification these include neurodegenerative diseases such as Parkinson's disease and Parkinson's-like syndromes such as progressive supranuclear palsy and multiple system atrophy, senile dementia such as Alzheimer's disease, depression, AIDS encephalopathy, multiple sclerosis, amyotrophie lateral sclerosis, migraine, attention deficit disorder, narcolepsy), sleep apnea or other disorders that cause excessive daytime sleepiness, Huntington's disease, cerebral ischemia, brain trauma, hepatic fibrosis, cirrhosis, and fatty liver.

The scope of the claims is not adequately enabled solely based on the activity of the compounds provided in the specification at pages 1 and 7. The instant compounds are disclosed have adenosine A_{2a} inhibitory or modulatory activity and it is recited that the instant compounds are useful in treating several diseases, for which applicants provide no competent evidence. Reading specification it appears that instant compound is useful for treating all sorts of diseases including central nervous system diseases such as Alzheimer's disease, Huntington's disease, dementia, amylotrophic lateral

sclerosis etc. for which applicants have not provided any experimental support. Moreover many if not most of central nervous system diseases such as Alzheimer's disease, ALS, multiple sclerosis etc. are very difficult to treat. For multiple sclerosis alone there is no known drug, which can successfully reverse the course of the disease, despite the fact that there are many drugs, which can be used for "inflammatory condition".

To "prevent" actually means to anticipate or counter in advance, to keep from happening etc. (as per Websters II Dictionary) and there is no disclosure as to how one skilled in the art can reasonably establish the basis and the type of subject to which the instant compounds can be administered in order to have the "prevention" effect. There is no evidence of record, which would enable the skilled artisan in the identification of the people who have the potential of becoming afflicted with the disease(s) or disorder(s) claimed herein.

That a single class of compounds can be used to prevent any or all diseases in general embraced in the claims is an incredible finding for which applicants have not provided supporting evidence.

Even a recent review of adenosine receptors suggest the use of these antagonists still under experimental stage and speculative in nature. See Baraldi et al., European Journal of Medicinal Chemistry 38: 367-382, 2003.

Note substantiation of utility and its scope is required when utility is "speculative", "sufficiently unusual" or not provided. See Ex parte Jovanovics, 211 USPQ 907, 909; In

re Langer 183 USPQ 288. Also note Hoffman v. Klaus 9 USPQ 2d 1657 and Ex parte Powers 220 USPQ 925 regarding type of testing needed to support in vivo uses.

Next, applicant's attention is drawn to the Revised Utility and Written Description Guidelines, at 66 FR 1092-1099, 2001 wherein it is emphasized that 'a claimed invention must have a specific and substantial utility'. The state of the art is indicative of the requirement for undue experimentation.

In evaluating the enablement question, several factors are to be considered. Note In re Wands, 8 USPQ2d 1400 and Ex parte Forman, 230 USPQ 546. The factors include: 1) The nature of the invention, 2) the state of the prior art, 3) the predictability or lack thereof in the art, 4) the amount of direction or guidance present, 5) the presence or absence of working examples, 6) the breadth of the claims, and 7) the quantity of experimentation needed.

1) The nature of the invention: Therapeutic use of the compounds in treating various central nervous diseases that require Adenosine A_{2a} inhibitory or modulatory activity.

2) The state of the prior art: A very recent publication expressed that the effects of Adenosine A_{2a} inhibitory activity are still in experimental stage and are unpredictable. See Baraldi et al. cited above.

3) The predictability or lack thereof in the art: Applicants have not provided any competent evidence or disclosed tests that are highly predictive for the pharmaceutical use for the treatment or prevention of all or any diseases by the instant compounds. Pharmacological activity in general is a very unpredictable area. Note that in cases involving physiological activity such as the instant case, "the scope of enablement

obviously varies inversely with the degree of unpredictability of the factors involved". See In re Fisher, 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970).

4) The amount of direction or guidance present and 5) the presence or absence of working examples: Specification has no working examples to show all diseases can be treated based on the test results of Adenosine A_{2a} inhibitory activity and the state of the art is that the effects of adenosine receptor antagonists are unpredictable.

6) The breadth of the claims: The instant claims as recited embrace treatment of any or all diseases as well as all central nervous system diseases.

7) The quantity of experimentation needed would be an undue burden to one skilled in the pharmaceutical arts since there is inadequate guidance given to the skilled artisan, regarding the pharmaceutical use, for the reasons stated above.

Thus, factors such as "sufficient working examples", "the level of skill in the art" and "predictability", etc. have been demonstrated to be sufficiently lacking in the instant case for the instant method claims. In view of the breadth of the claims, the chemical nature of the invention, the unpredictability of ligand-receptor interactions in general, and the lack of working examples regarding the activity of the claimed compounds towards treating the variety of diseases of the instant claims, one having ordinary skill in the art would have to undergo an undue amount of experimentation to use the instantly claimed invention commensurate in scope with the claims.

MPEP 2164.01(a) states, "A conclusion of lack of enablement means that, based on the evidence regarding each of the above factors, the specification, at the time the application was filed, would not have taught one skilled in the art how to make and/or

use the full scope of the claimed invention without undue experimentation. In re Wright, 999 F.2d 1557,1562, 27 USPQ2d 1510, 1513 (Fed. Cir. 1993)." That conclusion is clearly justified here. Thus, undue experimentation will be required to make Applicants' invention.

Allowable Subject Matter

Claims 23-25 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims. Said claims, barring finding of any prior art in a subsequent search, would be allowable as prior art search in the related area and prior art of record did not teach or suggest the compounds embraced in these claims.

Conclusion

Any inquiry concerning this communication from the examiner should be addressed to Venkataraman Balasubramanian (Bala) whose telephone number is (571) 272-0662. The examiner can normally be reached on Monday through Thursday from 8.00 AM to 6.00 PM. The Supervisory Patent Examiner (SPE) of the art unit 1624 is James O. Wilson, whose telephone number is 571-272-0661. The fax phone number for the organization where this application or proceeding is assigned (571) 273-8300. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (571) 272-1600.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAG. Status

information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-2 17-9197 (toll-free).

/Venkataraman Balasubramanian/

Primary Examiner, Art Unit 1624